Selenium Supplementation and the Effects on Reproductive Outcomes, Biomarkers of Inflammation, and Oxidative Stress in Women with Polycystic Ovary Syndrome

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Key words
- selenium
- supplementation
- polycystic ovary syndrome
- reproductive outcomes
- inflammation
- oxidative stress

Abstract

Selenium supplementation could be effective on reproductive outcomes, biomarkers of inflammation, and oxidative stress among women with polycystic ovary syndrome (PCOS). The aim of the study was to determine the effects of selenium supplementation on reproductive outcomes, biomarkers of inflammation, and oxidative stress in PCOS patients. The present randomized double-blind, placebo-controlled trial was conducted on 64 women aged 18–40 years old with PCOS at the clinic affiliated to Ardabil University of Medical Sciences, Ardabil, Iran. The participants were randomly assigned to 2 groups receiving either 200 µg selenium daily (n = 32) or placebo (n = 32) for 8 weeks. Hormonal profiles, biomarkers of inflammation, and oxidative stress were measured and compared both before and after the treatment. After 8 weeks of intervention, pregnancy rate in the selenium group was higher than in the placebo group: 18.8 (6/32) vs. 3.1 % (1/32), p = 0.04. In addition, alopecia (40.6 vs. 9.4 %, p = 0.004) and acne (46.9 vs. 12.5 %, p = 0.003) decreased following the consumption of selenium supplements compared with placebo. Additionally, patients who received selenium supplements had significantly decreased serum dehydroepiandrosterone (DHEA) levels (p = 0.02), hirsutism (modified Ferriman–Gallwey scores) (p < 0.001), serum high sensitivity C-reactive protein (hs-CRP) (p = 0.02), and plasma malondialdehyde (MDA) levels (p = 0.01) compared with placebo. We did not observe any significant effects of taking selenium supplements on other hormonal profiles, nitric oxide (NO), and other biomarkers of oxidative stress. Taken together, selenium supplementation for 8 weeks among PCOS women had beneficial effects on reproductive outcomes, DHEA, hs-CRP, and MDA levels.

Supporting Information for this article is available online at http://www.thieme-connect.de/products.

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Abbreviations

β-HCG	β-Human chorionic gonadotropin
CVD	Cardiovascular disease
DHEA	Dehydroepiandrosterone
FRAP	Ferric reducing antioxidant power
FSH	Follicular-stimulating hormone
FOH	Functional ovarian hyperandrogenism
GSH	Glutathione
GSH-Px	Glutathione peroxidase
Hs-CRP	High-sensitivity C-reactive protein
ITT	Intention-to-treat
LH	Luteinizing hormone
LOCF	Last Observation Carried Forward
MDA	Malondialdehyde
MUFA	Monounsaturated fatty acid
NO	Nitric oxide
OCPs	Oral contraceptives
PCOS	Polycystic ovary syndrome
PUFA	Polyunsaturated fatty acid
ROS	Reactive oxygen species
RDA	Recommended Dietary Allowances
RA	Rheumatoid arthritis
SIRS	Systemic inflammatory response syndrome
SFA	Saturated fatty acid
TAC	Total antioxidant capacity
TAS	Total antioxidant status
T2DM	Type 2 diabetes mellitus
TNF-α	Tumor necrosis factor alpha
TDF	Total dietary fiber
tT	Total testosterone

Introduction

Polycystic ovary syndrome (PCOS) is a common endocrine and metabolic aberration [1], affecting 5–10 % of women of childbearing age in worldwide [2]. Previous studies have shown that PCOS

is the most prevalent cause of female infertility, which is characterized by ovarian hyperandrogenism and chronic anovulation [3]. In addition, due to increased production of free radicals and reactive oxygen species (ROS) [4], elevated circulating protein carbonyls, tumor necrosis factor-α (TNF-α), and decreased insulin signaling [5,6], it is associated with increased biomarkers of inflammation and oxidative stress. Increased inflammatory factors and biomarkers of oxidative stress among patients with PCOS may predict the development of cardiovascular disease (CVD) and type 2 diabetes mellitus (T2DM) [7–9].

Recent studies have reported that the use of insulin-sensitizing drugs including metformin, rosiglitazone, and pioglitazone improves ovulation by improving clinical and biochemical features of patients diagnosed with PCOS [10]. Selenium is an essential trace element, which has importance to human biology and health. More recently, evidence has also been presented that selenium may affect several reproductive and obstetric complications including male and female infertility [11]. Furthermore, current data supports the beneficial effect of selenium supplementation on metabolic profiles and biomarkers of oxidative stress among patients with PCOS [12,13]. Valenta et al. [14] demonstrated that high-dose selenium supplementation for 14 days (1000 µg on day 1 and 500 µg/day on days 2–14) decreased plasma CRP levels in patients with systemic inflammatory response syndrome (SIRS)/sepsis. Increased erythrocyte and plasma total antioxidant status (TAS), reduced glutathione (GSH), and glutathione peroxidase (GSH-Px) were also seen following the intake selenium supplements in patients with epilepsy and refractory epilepsy [15]. However, no significant change in malondialdehyde (MDA) concentrations was seen after the consumption of selenium supplements in rats [16].

Beneficial effects of selenium supplementation on improved reproductive outcomes, biomarkers of inflammation, and oxidative stress might be attributed to its inhibitory effect on augmentation of proinflammatory cytokines and reactive oxygen species/reactive nitrogen species [17,18]. Borderline selenium status is high among healthy Iranian women. Rafraf et al. [19] reported that 69 women have serum selenium concentrations under 80 µg/l. Although there is no specific data on mean daily intake of selenium in Iranian women with PCOS, the mean of selenium consumption among postmenopausal women was significantly less than the Recommended Dietary Allowances (RDA) [20]. Considering these points, we hypothesized that selenium supplementation might affect reproductive outcomes, biomarkers of inflammation, and oxidative stress in patients with PCOS. We are aware of no such study among PCOS women. This study was thus aimed to investigate the effect of selenium supplementation on reproductive outcomes, biomarkers of inflammation, and oxidative stress of PCOS women.

Subjects and Methods

Participants

Sixty four women with PCOS from October 2014 to December 2014 were included in the patients attending the outpatient clinic of the Infertility Research Center of Ardabil Medical University. The current study was approved by the Institutional Review Board at Ardabil University of Medical Sciences (AUMS). Informed written consent was obtained from all participants. This study was done based on the guidelines laid down in the Declaration of Helsinki. The trial was registered in the Iranian website (www.irct.ir) for registration of clinical trials (IRCT code: IRCT201412295623N33). The diagnosis of PCOS was according to European Society for Human Reproduction and Embryology/American Society for Reproductive Medicine guidelines (Rotterdam criteria, 2003), as including at least 2 of the following 3 criteria: 1) oligo- and/or anovulation as the presence of chronic amenorrhea or a menstrual cycle length of less than 21 days or more than 35 days, or more than 4 days variation between cycles; 2) clinical or biochemical signs of hyperandrogenism; and 3) polycystic ovary morphology shown on ultrasound examination, defined as 12 or more small follicles [21]. Our inclusion criteria were age between 18 and 40 years with PCOS according to Rotterdam criteria. In the current study, we excluded patients who had elevated levels of prolactin, thyroid disorder, or T2DM and congenital adrenal hyperplasia. In addition, all PCOS women had normal baseline renal function tests, bilirubin, and aminotransferases. During the last 3 months before the intervention, none of the study patients used any form of oral contraceptives (OCPs), other steroid hormones, or any other treatments likely to affect ovarian function, insulin sensitivity, or inflammatory factors, biomarkers of oxidative stress as well as nutritional supplements.

Study design

At the first trial and after stratification for pre-supplementation BMI (< 25 and ≥ 25 kg/m^2) and age (< 30 and ≥ 30 years), patients with PCOS were randomly divided into 2 groups. Group 1 received 200 µg daily selenium tablet as selenium yeast (n = 32) and group 2 received the placebo (n = 32) for 8 weeks. Selenium supplements and its placebos (cellulose) were manufactured by Nature Made Pharmaceutical Company (California, USA) and Barij Essence Pharmaceutical Company (Kashan, Iran), respectively. Supplements and placebos were in the same form of package and the patients and researcher were not conscious of the content of the pack until the end of trial. In addition, all patients with PCOS took metformin at the initial dose of 500 mg, which was elevated in a stepwise manner during the first 3 weeks to incorporate the side effects until the patients were taking a total of 1 500 mg/day. Patient allocation and block size were obtained using random number tables. At the time of randomization, sequentially numbered, sealed envelopes were opened. Allocation to study group was concealed until the main analyses were completed. The randomized allocation sequence, enrolling participants, and assigning participants to interventions were done by a trained midwife at gynecology clinic. At the beginning study, the subjects were requested to keep their usual diet and level of physical activity throughout the study period as well as not to receive any anti-inflammatory medications, supplements, and other medications that might affect their reproductive physiology during the 8-week intervention. The use of selenium supplements and placebos throughout the study was checked through asking participants to bring the medication containers. To increase the compliance, all patients were receiving short messages on their cell phones to take the supplements each day. All participants provided 3 dietary records (1 weekend day and 2 weekdays) and 3 physical activity records at week 2, 4, and 6 of intervention to make sure that they maintained their usual diet and physical activity during intervention. The dietary records were based on estimated values in household measurements. In the current study, we used Nutritionist IV software (First Databank, San Bruno, CA, USA) adjusted for Iranian foods to take macro and micronutrients intakes of patients according to 3-day food diaries.

Assessment of variables

All participants were evaluated at baseline study on the third day of a spontaneous or progesterone-induced menstrual cycle. Anthropometric assessments included determinations of height, weight (Seca, Hamburg, Germany), and body mass index (BMI). Clinical assessments included determinations of hirsutism using modified Ferriman-Gallwey scores [22], of acne score [23], and of alopecia based on assessment guidelines collated by Olsen et al. [24]. Acne was marked by a 4-point scale: 0, no acne; 1, minor acne on face; 2, moderate acne on face only; and 3, severe acne, face and back or chest. In case of missed menstrual period, we checked β-human chorionic gonadotropin (β-HCG) to detect pregnancy a week after the missed period. If β-HCG levels were higher than 25 (by the Vidas method), the patient was pregnant and medications discontinued. Fasting blood samples (10 ml) were collected before and 8 weeks after of the intervention at Ardabil reference laboratory in an early morning after an overnight fast. Blood was collected in 2 separate tubes: 1) one without EDTA to separate the serum, in order to quantify serum prolactin, follicular-stimulating hormone (FSH) and luteinizing hormone (LH), free testosterone, dehydroepiandrosterone (DHEA) and high sensitivity C-reactive protein (hs-CRP) levels and 2) another one containing EDTA to examine plasma nitric oxide (NO) and biomarkers of oxidative stress. Blood samples were immediately centrifuged (Hettich, 78 532 Tuttlingen, Germany) at 3 500 rpm for 10 min to separate the serum. The samples were then stored at −70 °C until being analyzed at the AUMS reference laboratory. Commercial kits were used to measure serum prolactin, FSH and LH concentrations (Pars Azmun, Tehran, Iran). All inter- and intra-assay CVs for prolactin, FSH and LH measurements were less than 7 %. Serum free testosterone, DHEA, and 17-OH progesterone concentrations were determined by using commercial kits (Monobind, CA, USA). Serum hs-CRP was quantified using an ELISA kit (LDN, Nordhorn, Germany) with intra- and interassay CVs of 2.9 and 4.8 %, respectively. The plasma NO concentration was determined by the Griess method [25]. Plasma total antioxidant capacity (TAC) was assessed by the use of the ferric reducing antioxidant power (FRAP) method developed by Benzie and Strain [26]. Plasma GSH was examined using the method of Beutler et al. [27]. The plasma MDA levels were determined by the thiobarbituric acid reactive substance spectrophotometric test [28]. CVs for plasma TAC, GSH and MDA were 1.1, 2.8, and 3.7 %, respectively.

Statistical methods

We used the Kolmogrov-Smirnov test to examine if variables were normally distributed. Intention-to-treat (ITT) analysis of the primary study end-point was performed for all the randomly assigned participants. Missing data from dropped out participants were imputed using the method of "Last Observation Carried Forward (LOCF)". The Pearson chi-square test was used to compare categorical variables. Independent sample Student's *t*-test was used to detect differences in general characteristics and dietary intake between the 2 groups. To determine the effects of selenium supplementation on hormonal profiles, inflammatory factors and biomarkers of oxidative stress, one-way repeated-measures ANOVA was used to evaluate the between-group changes in variables during the study. In this analysis, the treatment was regarded as between-subject factor and time with 2 time-points (baseline and 8 weeks after of the intervention) was considered as within-subject factor. To assess if the magnitude of the change in dependent variables depended on the baseline age and BMI, we controlled all analyses for baseline values of age and BMI to avoid potential bias. These analyses were also done using one-way repeated measures ANOVA. A p-value < 0.05 was considered statistically significant. All statistical analyses were done using the Statistical Package for Social Science version 17 (SPSS Inc., Chicago, IL, USA). In the current study, the primary endpoint variables were biomarkers of oxidative stress including plasma TAC, GSH, and MDA levels. To calculate the sample size, we used the standard formula suggested for parallel clinical trials by considering type one error (α) of 0.05 and type 2 error (β) of 0.20 (power = 80 %). Based on a previous study [29], we used 2.19 µmol/l as SD and 2.80 µmol/l as the difference in mean (d) of MDA levels as key variable. Based on this, we reached to 27 patients in each group. Assuming a dropout of 5 patients per group, the final sample size was determined to be 32 patients per group.

Results

Baseline evaluations and dropouts

In the current study, 64 women with PCOS met the inclusion criteria based on Rotterdam criteria and were enrolled in the study. Among the individuals in the selenium group, 2 women [withdrawn due to personal reasons (n = 2)] and in the placebo group, 2 women [withdrawn due to personal reasons (n = 2)] did not complete the trial. However, as the analysis was done according to ITT protocol, all 64 patients with PCOS were included in the end analysis. On the average, the rate of compliance in our study was high, such that > 90 % of tablets were taken throughout the study in both groups. No side effects were reported following the administration of selenium supplements in patients with PCOS throughout the study.

General characteristics of study participants

Mean age (25.1 ± 4.5 vs. 25.4 ± 4.9 years, p = 0.85), baseline BMI (24.7 ± 3.5 vs. 25.3 ± 4.3 kg/m^2, p = 0.53), and end-of-trial BMI (24.3 ± 3.5 vs. 25.1 ± 4.2 kg/m^2, p = 0.47) were not significantly different between selenium and placebo groups.

Dietary intakes of study participants throughout the study

According to the 3-day dietary records taken throughout the intervention, any significant change was not seen between the 2 groups in terms of dietary intakes of energy, carbohydrates, proteins, fats, saturated fatty acids (SFAs), polyunsaturated fatty acids (PUFAs), monounsaturated fatty acids (MUFAs), cholesterol, total dietary fiber (TDF), selenium, magnesium, manganese, vitamins C and E (data not shown).

Clinical outcomes

After 8 weeks of intervention, pregnancy rate in the selenium group was higher than in the placebo group: 18.8 (6/32) vs. 3.1 % (1/32), p = 0.04 (**Table S1**). In addition, alopecia (40.6 vs. 9.4 %, p = 0.004) and acne (46.9 vs. 12.5 %, p = 0.003) decreased following the consumption of selenium supplements compared with placebo.

The effect of selenium supplementations on biochemical measurements

Patients who received selenium supplements had significantly decreased serum DHEA levels (p = 0.02), hirsutism (p < 0.001),

serum hs-CRP (p = 0.02), and plasma MDA levels (p = 0.01) compared with placebo (**Table 1**). We did not observe any significant effects of taking selenium supplements on other hormonal profiles, NO, and other biomarkers of oxidative stress. We controlled the baseline levels in the analyses. However, after adjustment no significant changes in our findings occurred, except for FSH (p = 0.03) and DHEA levels (p = 0.12).

Adjusted changes in biochemical measurements

Additional adjustments for age and baseline BMI did not affect our findings, except for FSH (p = 0.03) and DHEA levels (p = 0.13) (**Table S2**).

A summary of patient flow diagram is presented in **Fig. S1**.

Discussion

We revealed for the first time that selenium supplementation in PCOS women resulted in a significant increase in pregnancy rate, a decreased reduction in alopecia, acne, DHEA, hirsutism, hs-CRP and MDA levels. It must be considered that mean dietary plus supplemental selenium intake was lower in our study patients than upper limits (400 µg). However, data on the effects of selenium supplementation on toxicity/teratogenicity even in subjects with high dietary selenium intake are conflicting. For instance, some of the subjects in Burk et al study [30] ingested >800 µg selenium/d for 16 weeks. However, this is considerably more than the Institute of Medicine's tolerable upper level of 400 µg/d [31], no signs of selenium toxicity in mentioned study were observed. In another study by Reid et al. [32] more subjects on 3200 µg/day have reported symptoms of selenium toxicity.

Women with PCOS are susceptible to infertility, hirsutism, increased inflammatory factors and increased biomarkers of oxidative stress [33]. Our study demonstrated that taking selenium supplements for 8 weeks in women with PCOS resulted in a significant increase in pregnancy rate, a significant reduction in alopecia and acne compared with placebo. Data regarding favorable effects of selenium intake and female fertility are scarce. In line with our study, conception rate following the intake of 50 mg/ml selenium as barium selenate was higher than in the control ewes [34]. In addition, fertility has been improved by supplemental co-administration of vitamin E and selenium in cattle [35]. Paszkowski et al. [36] reported that patients with unexplained infertility had a significant decrease in follicular selenium concentrations compared with patients with tubal infertility. Furthermore, a recent study has shown lower levels of serum and follicular fluid selenium in women undergoing in vitro fertilization treatment compared with nonpregnant control women [37]. Edassery et al. [38] reported that women with unexplained infertility or premature ovarian failure have significantly increased serum levels of the ovarian autoantibody protein, selenium binding protein-1. However, some researchers have not found association between herd selenium concentrations and fertility parameters [39]. Previous studies have reported that selenium intake is associated with decreased biomarkers of oxidative stress and insulin resistance in women with PCOS [12,13]. Antioxidants are compounds that are capable of disposing or suppressing the formation of ROS, free radicals, and lipid hydroperoxides [40]. However, no study has directly evaluated the effects of oxidative stress on fertility in women; a recent review has reported that antioxidants may influence female reproduction [41]. In addition, insulin resistance in patients with PCOS influences the developmental potential of human immature oocytes, as indicated by impaired oocyte maturation, fewer fertilized oocytes, and cleaved embryos [42,43].

Results of the present study show that selenium supplementation among PCOS women decreased serum DHEA levels and hirsutism, while did not affect other hormonal profiles. As this study is among the first that reports the effect of selenium supplementation on hormonal profiles among women with PCOS, we did not compare findings of the current study with others although few studies assessed the association between selenium levels and hormonal profiles in women with PCOS. For instance, Coskun et al. [44] reported decreased plasma concentrations of selenium and a negative association between selenium and LH, total testosterone (tT) in PCOS women, indicating that selenium may play a role in the pathogenesis of PCOS related with hyper-

Table 1 The effect of selenium supplementations on hormonal status, biomarkers inflammation and oxidative stress.

	Placebo group (n = 32)			Selenium group (n = 32)			p *
	Week 0	Week 8	Change	Week 0	Week 8	Change	
Prolactin (mIU/l)	643.27 ± 376.31	546.11 ± 262.97	−97.15 ± 443.26	697.01 ± 614.53	743.28 ± 585.41	46.26 ± 337.43	0.15
FSH (IU/l)	7.92 ± 2.85	8.40 ± 3.05	0.48 ± 2.55	6.39 ± 3.17	6.15 ± 3.38	−0.24 ± 4.28	0.41
LH (IU/l)	13.67 ± 13.53	11.48 ± 7.72	−2.19 ± 13.77	10.93 ± 8.21	10.60 ± 8.94	−0.33 ± 10.21	0.54
Free testosterone (pg/ml)	3.24 ± 1.77	3.02 ± 1.66	−0.21 ± 0.92	2.70 ± 1.51	2.41 ± 1.46	−0.28 ± 1.15	0.78
DHEA (µg/ml)	1.59 ± 0.72	1.56 ± 0.73	−0.02 ± 0.41	2.01 ± 0.80	1.65 ± 0.85†	−0.36 ± 0.73	0.02
17-OH Progesterone (ng/ml)	2.00 ± 1.39	1.76 ± 1.28	−0.23 ± 1.68	2.39 ± 2.01	1.92 ± 1.82	−0.46 ± 2.56	0.66
mF-G scores	8.34 ± 6.30	8.12 ± 6.24	−0.21 ± 0.83	12.46 ± 7.21	10.12 ± 5.45†	−2.34 ± 2.57	< 0.001
hs-CRP (ng/ml)	2572.26 ± 2506.08	2765.81 ± 2372.19	193.54 ± 1117.45	2184.06 ± 2693.84	1472.70 ± 1444.43†	−711.35 ± 1959.37	0.02
NO (µmol/l)	57.15 ± 17.09	57.22 ± 16.98	0.07 ± 23.38	46.91 ± 7.59	50.76 ± 14.75	3.85 ± 13.37	0.43
TAC (mmol/l)	696.45 ± 137.43	692.13 ± 138.74	−4.32 ± 200.88	823.14 ± 195.00	803.60 ± 147.74	−19.54 ± 135.00	0.72
GSH (µmol/l)	437.30 ± 107.12	472.35 ± 148.66	35.05 ± 168.55	476.64 ± 122.77	459.92 ± 120.73	−16.72 ± 132.53	0.17
MDA (µmol/l)	4.40 ± 2.71	5.8 ± 3.03†	1.40 ± 3.11	4.95 ± 1.25	4.81 ± 1.36	−0.13 ± 1.03	0.01

All values are means ± SDs

* Obtained from repeated measures ANOVA test (time × group interaction)

DHEA: Dehydroepiandrosterone; FSH: Follicle-stimulating hormone; GSH: Glutathione; Hs-CRP: High sensitivity C-reactive protein; LH: Luteinizing hormone; mF-G: Modified Ferriman-Gallwey; MDA: Malondialdehyde; NO: Nitric oxide; TAC: Total antioxidant capacity

† Significant difference with baseline study

androgenism. Selenium supplementation may result in decreased serum DHEA levels and hirsutism through improved markers of insulin metabolism [13] and decreased oxidative stress [12]. Previous studies have demonstrated that a positive association between hyperandrogenism, hyperinsulinemia, and insulin resistance in females with elevated androgen levels due to PCOS [45,46]. In addition, oxidative stress is directly correlated with both insulin resistance and hyperandrogenism, which in turn contribute to endocrine and biochemical alterations in women with functional ovarian hyperandrogenism (FOH) [47].

The present study revealed that taking selenium supplements in PCOS patients for 8 weeks was associated with decreased serum hs-CRP levels, but did not affect plasma NO concentrations. Supporting with our study, administration of selen plus supplements contained 50 µg selenium, 8 mg zinc, 400 µg vitamin A, 125 mg vitamin C, and 40 mg vitamin E daily has reduced hs-CRP concentrations among rheumatoid arthritis (RA) for 12 weeks [48]. In addition, high-dose selenium supplementation for 14 days (1 000 µg on day 1 and 500 µg/day on days 2–14) has led to a significant decrease in plasma CRP levels in patients with SIRS/sepsis [14]. Unlike, no significant effect on hs-CRP levels was observed after intake of cereal biscuit with selenized onion, curcuma, and green tea for 2 months among healthy adults [49]. Similar finding was also seen in centrally obese women who consumed 200 µg selenium supplements for 6 weeks [50]. Increased inflammatory factors in patients with PCOS render them at a potential increased risk for the development of atherosclerosis, T2DM, cancer, infertility, and other comorbidities [51]. Selenium intake may decrease serum hs-CRP levels through inhibiting the activation of NF-kappa B by modulating selenoprotein genes expression [52] and increasing selenoprotein biosynthesis which in turn results in suppressed CRP production [53].

We found that selenium supplementation among women with PCOS has resulted in a significant reduction in plasma MDA levels, but it could not affect plasma TAC and GSH levels. Similarly, Salehi et al. [54] demonstrated a significant decrease in MDA levels after administration of 200 µg selenium supplements per day for 12 weeks among hemodialysis patients. Furthermore, vitamin E-plus-selenium combination decreased MDA concentrations in streptozotocin-induced diabetic rats [55]. Supplementation with 200 µg selenium per day for 3 weeks did not influence biomarkers of oxidative stress including TAS and GSH levels among overweight adults [56]. However, few researchers did not observe such effects of selenium supplementation on MDA levels. For instance, any significant change in MDA levels was not observed after taking selenium supplements in rats [16]. Previous studies have shown that oxidative stress in female reproduction is associated with polycystic ovarian syndrome and endometriosis [57]. Needless to say, these pathologies negatively influence pregnancy rates and IVF outcomes. Selenium is an essential component of the erythrocyte GSH-Px system [58], which functions as part of an antioxidant defense to protect polyunsaturated fatty acids, the damaging effects of free radicals, and lipid hydroperoxides such as MDA [59]. In addition, selenium might decrease hydroperoxides levels via inhibiting production of proinflammatory cytokines and reactive oxygen species/reactive nitrogen species [17].

Taken together, selenium supplementation for 8 weeks among PCOS women had beneficial effects on reproductive outcomes, DHEA, hs-CRP and MDA levels.

Author Contributions

Z.A. contributed in conception, design, statistical analysis, and drafting of the manuscript. M.R, M.J., Z.F., Z.H., M.M., Y.Gh. and T.B. contributed in data collection and manuscript drafting.

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Conflict of Interest

None of the authors had any personal or financial conflict of interest.

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